REMARKS

Claims 1-66 are pending in this application. Claims 1-11 and 56-66 have been examined and claims 12-55 have been withdrawn from consideration as being drawn to nonelected subject matter. Claims 1-2 and 5-7 were rejected under 35 U.S.C. § 102(b) and claims 1-11 and 56-66 were rejected under 35 U.S.C. § 103.

By this amendment, claims 1-11 and 56 have been amended without prejudice or disclaimer of any previously claimed subject matter. Support for the amendment to claims 1-11 and 56 can be found, *inter alia*, throughout the specification and, for example, at page 6, lines 21-21 and at page 49, lines 21-23.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Rejection under 35 U.S.C. §102(b)

Claims 1-2 and 5-7 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Uhlen, U.S. Pat. No. 5,629,158. Applicants respectfully traverse this rejection.

As amended, the claimed invention is directed to a pharmaceutical composition comprising complexes which comprise an immunomodulatory polynucleotide (IMP) linked to a nonbiodegradable microcarrier. The IMP comprises an immunostimulatory sequence (ISS) and the ISS comprises the sequence 5'-CG-3'. The claimed invention is also directed to kits comprising

such complexes. Upon administration to an individual, the complexes of the invention modulate an immune response in the recipient.

Uhlen describes a method and kit for use in diagnosis of a medical condition involving identification of a specific DNA sequence. As part of this diagnostic method, the target DNA is amplified and then immobilized on a solid support where the target DNA can be subjected to further *in vitro* operations such as further PCR amplification, DNA sequence determination and *in vitro* mutagenesis procedures. Uhlen, Column 5, lines 20-51. Thus, the teachings of Uhlen involve the use of a DNA-support complex in diagnostic or research procedures performed *in vitro*.

For a claim to be anticipated by a reference, the reference much teach each and every element of the claim. Uhlen does not teach the use of the complexes for administration to an individual or as a component of a pharmaceutical composition. Accordingly, Applicants respectfully submit that the Uhlen does not anticipate the claimed invention.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b).

Rejection under 35 U.S.C. §103

Claims 1-11 and 56-66 were rejected under 35 U.S.C. §103 as allegedly being unpatentable over Schwartz, *et al.* (WO 98/55495, "Schwartz") in view of the combined teachings of Schreiner *et al.* (U.S. Pat. No. 6,352,975, "Schreiner"), Nantz *et al.* (U.S. Pat. No. 5,824,812, "Nantz") and Uhlen. Applicants respectfully traverse this rejection.

A *prima facie* case of obviousness requires that three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim

limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20USPQ2d 1438 (Fed. Cir. 1991); MPEP §2143. If any one of these three criteria is not met, a *prima facie* case of obviousness has not been established. As presented below, Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

The claimed invention is directed to a pharmaceutical composition comprising an immunomodulatory polynucleotide/microcarrier (IMP/MC) complex as described above, and a kit comprising an IMP/MC complex and a pharmaceutically acceptable excipient for use in immunomodulation of an individual.

Applicants have previously described the teachings of Schwartz on the record. Schreiner describes gene therapy methods for treating hypertension in which an expression vector encoding an angiogenic factor is delivered to cells and the expression of the angiogenic factor by the cells results in treating hypertension. Schreiner lists in variety of ways for delivery the vector to the cells, including with a microparticle. Nantz describes polynucleotide complexes for cell delivery but is silent with regard to non-biodegradable complexes. As discussed above, Uhlen describes DNA immobilized on a solid support for *in vitro* diagnostic procedures.

There is no suggestion or motivation in the references or in the art to combine Schwartz with the secondary references to arrive at the claimed invention.

Schwartz is directed to stimulation an immune response through administration of particular immunostimulatory polynucleotide complexes. The immunostimulatory polynucleotide sequences of Schwartz need not encode a polypeptide nor be expressed in the recipient to accomplish the desired effect. Schreiner is directed to gene therapy which involves introducing to a recipient a polynucleotide encoding an angiogenic factor, expressing the factor and stimulating angiogenesis in the recipient with the expressed factor. Since Schwartz and Schreiner are directed to nonanalogous subject matter, there is no motivation in either reference to combine their

teachings. Applicants also submit that one skilled in either of the gene therapy or the immune modulation arts would not look to the teaching of Schwartz or Schreiner, respectively, to modify the teaching of the other.

The teaching of Uhlen is directed to *in vitro* procedures and methods of DNA analysis and Uhlen does not teach or suggest administration of the DNA-support complex to an individual, much less administration of the DNA-support complex to modulate a response in a recipient. The teaching of Uhlen provides no suggestion of desirability of making the combination with Schwartz. Accordingly, there is no motivation in the references or in the art to combine the teachings of Schwartz and Uhlen to arrive at the claimed invention.

Nantz describes polynucleotide cytofectin complexes for delivery of polynucleotides to cells but does not teach or suggest the use of non-biodegradable complexes for this purpose. In fact, Nantz only mentions complex degradability when discussing the improvements associated with the cytofectin complexes and Nantz points out that problems with well-known lipofectin complexes include "non-metabolizable ether bonds" (column 2, lines 26-29). Accordingly, there is no motivation in the references or in the art to combine the teachings of Schwartz and Nantz to arrive at the claimed invention. Further, even if the teachings of Nantz and Schwartz were combined, there is no teaching of the claimed invention, and thus, again, no *prima facie* case of obviousness.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). A statement that modifications of the prior art to meet the claimed invention would have been " 'well within the ordinary skill of the art at the time the claimed invention was made' " because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex*

parte Levengood, 28 USPQ2d 1300 (BPAI 1993). See also *In re Kotzab* 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000). MPEP §2143.01.

Thus, Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §103.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 377882001700.

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Respectfully submitted,

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